

OCCUPATIONAL DERMOPATHIES AND JUDGMENT OF SUITABILITY

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ABSTRACT

Occupational dermatosis is defined as a skin pathology expressed as a result of factors mainly associated with the work environment. Given the considerable heterogeneity of skin pathologies that are possible in the work environment, it was decided not to use the term dermatitis but dermatosis, which is generic but more appropriate for such pathological conditions. Many occupational activities can lead to skin diseases, especially when the exposure is very intense, such as the construction industry, the metal industry, the chemical industry, etc. In many developed countries, including the countries of the European Union, occupational skin diseases are the second most common occupational disease, after musculoskeletal disorders. The high incidence of such diseases is attributable to tens of thousands of chemicals used in the workplace in different formulations, such as solvents, heavy metals, benzene, cleaning products, pesticides, etc. The purpose of our review is to provide precise guidance on how to perform proper health surveillance. Health surveillance of workers exposed to any occupational sensitizing agent is intended to identify any individual factors of hypersusceptibility during preventive examinations, and preclinical signs during periodic examinations, to allow early diagnosis of disease by means of level 2 diagnostic testing. The judgments of suitability issued, also in order to safeguard the specific professionalism of the worker, must as far as possible resort to measures based on "prescriptions" motivated and feasible, not limitations equivalent to changes of job and therefore not feasible.

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1. Introduction

Occupational dermatosis is defined as "a skin pathology expressed as a result of factors mainly associated with the work environment" [1]. The district concerned is the skin surface, an organ with an extension of approximately 1.8 m² that represents the first line of defense against a multitude of external pathogens and environmental insults of various kinds. [2].

Given the considerable heterogeneity of skin pathologies that are possible in the work environment, it was decided not to use the term dermatitis but dermatosis, which is generic but more appropriate for such pathological conditions, especially for chronic conditions.

We know that the three basic criteria for defining a skin disorder as professional are as follows:

1. The pathology must have developed during professional activity;
2. Clinical manifestations are expected to improve if the patient is removed from the suspected work activity and suffer a recrudescence on return to work (positive stop-start test);
3. It must be possible to identify a plausible aetiological agent in the working environment that can be linked to the onset of skin manifestations.

Many occupational activities can lead to skin diseases, especially when exposure is very intense.

Some of the occupational sectors particularly at risk are:

- Construction sector
- Metal industry
- Chemical industry

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- Meat processing
- Production of cement products
- Hairdressing salons
- Health sector
- Agriculture
- Cleaning companies
- All areas where glues or other chemicals are handled.

The direct causes of occupational dermatoses are, in order of frequency:

1. Chemicals
2. Mechanical Stress
3. Physical
4. Organic

It should be noted that during the SARS COV 2 pandemic, many adverse skin reactions, including irritant dermatitis, allergic dermatitis and contact urticaria, were caused by the use of different types of protective gloves, including latex gloves, in different occupational groups [3-6]. In fact, although the use of protective gloves and masks reduced the risk of SARS COV 2 infection, it increased the incidence of skin manifestations.

In many developed countries, including the countries of the European Union, occupational skin diseases are the second most common occupational disease, after musculoskeletal disorders. At the European level they account for between 10 % and 20 % of recognised occupational diseases [7-8].

The high incidence of such diseases is attributable to tens of thousands of chemicals used in the workplace in different formulations, such as solvents, heavy metals, benzene, cleaning products, pesticides, etc., especially if used unintentionally without gloves, as in the case of mechanics or port workers [9]. The skin is the preferred route for absorbing these products, which cause oxidative stress with the production of free radicals that can subsequently alter cellular macromolecules such as DNA and RNA [10].

These factors are responsible for 80-90% of skin pathologies, but predisposing factors that cause these alterations also include biological agents (plants, phototoxic agents, irritants, animal proteins), physical agents (UV radiation, especially in prolonged exposure) [11] and autoimmune factors. [12].

Occupational dermatoses account for about 20-40% of work-related diseases; they are quite frequent pathologies within the framework of occupational diseases and are still one of the main causes of application for benefits by INAIL both for temporary absolute and permanent disability. [13].

The most frequent occupational skin lesions, after hand injuries, events that occur frequently in workers during industrial cleaning, painting, and lubrication, are contact dermatitis, accounting for about 90% of all skin disorders, the most frequent of which are irritant contact dermatitis (ICD), followed by allergic contact dermatitis (ACD) [14].

Specifically, the three main groups of occupational skin diseases are:

1. Irritations (including chemical burns, urticaria, etc.); these comprise about 80% of skin diseases;
2. Allergies (their incidence rate is constantly increasing); allergies comprise more than 10% of skin diseases;
3. Neoplasms, folliculitis, parasitosis, dyschromia and photo dermatitis.

In 80% of cases, these diseases affect the hands, the workers' main 'tool' [15].

The purpose of this review is to provide a guideline, designed to give precise guidance on how to deal with this occupational clinical condition, in order to issue a correct work eligibility.

2. Material and methods

We searched and analyzed evidence-based guidelines and abstracts, systematic reviews, and recent experimental research on the correlation and pathophysiologic mechanisms of occupational dermatitis. Key words used were "Occupational skin diseases," "Occupational dermatoses," "Allergic contact dermatitis (ICD)," "Irritative contact dermatitis (ACD)," "Cutaneous neoplasms," "Atopic dermatitis," and "Atopy." Through this strategy, more than 300 useful articles were identified using two primary sources to highlight relevant information, the PubMed and Google Scholar electronic databases. In addition to articles and reviews obtained from the databases, relevant articles and websites were considered as potential sources of information.

3. Results and discussion

3.1 Health surveillance

It concerns all workers exposed or to be exposed to any occupational sensitising agent known to be a skin irritant or which has been considered as part of the risk assessment [16-17] carried out under Legislative Decree 81/08, regardless of its inclusion in the tables annexed to the laws enforced in Italy, who must therefore be subject to health surveillance.

The aim of health surveillance of these workers is to identify individual hypersusceptibility factors during preventive examinations, and preclinical signs during periodic examinations, to enable early diagnosis of the disease by means of second level diagnostic tests.

Health surveillance should be particularly careful during the first periods of exposure, roughly the first two years, when the likelihood of developing sensitisation appears highest [18].

This has been reported for respiratory sensitisation, but can also be related to skin sensitisation. According to the literature, the indicative average induction period for different activities varies, for example, from 2 years in hairdressers, 3 years in food workers, 4 years in health care and metalworkers.

3.2 Diagnostic procedure

The suggested methodology to be followed and applied in the presence of hypersusceptibility or skin pathologies caused or aggravated by the work activity, or predisposing to the appearance of occupational dermatoses, must be based on a careful analysis of the activities carried out, even if reported as a generic risk in the risk assessment document, and on the preparation of a correct health protocol [19-20].

Finally, other predisposing factors should not be overlooked, such as poor working conditions in terms of hygiene, inadequate prevention and protection systems [21] or the presence of stressful psychological events, in its occupational forms, as a consequence of, for example, straining [22] (which is a mitigated form of mobbing, in which the continuity of the harassing actions is not guided by discriminatory intent); or from working night shifts, where, in particularly susceptible individuals, the alteration of the circadian rhythm and the increase in cortisol levels may be the cause of eczematous stress manifestations [22-25]. Finally, it should be remembered that increased cortisol levels may also be caused by intense and prolonged competitive sporting activity [26].

In particular, the health surveillance process involves:

1. Job analysis:

- Verification of exposure to chemical/physical, irritating, sensitising or triggering/aggravating factors for the pathology under investigation;
- Mode and duration of exposure, paying particular attention to any shifts, including night shifts, and rest period from any exposure;
- Possibility of preventive environmental interventions and/or use of PPE;
- Assessment of triggering or aggravating factors;

2. Medical examination

- Clinical history
- Objective examination
- Clinical and aetiological diagnosis

3.3 Medical history

The diagnosis is based, first of all, on an accurate anamnesis evaluating all individual risk factors, then the presence of non-occupational factors such as the use of accessories containing metals including nickel/cadmium/cobalt, or the use of particularly aggressive detergents, which can cause localised or systemic skin manifestations such as:

1. Atopy: Atopic dermatitis, respiratory allergy (rhinitis, asthma), asymptomatic sensitisation;
2. Extra-occupational skin disorders;
3. Sensitisation by pre-existing contact with ubiquitous haptens or previous exposure and sensitisation to the same risk factor.
4. Systemic pathologies.

3.3.1 Atopia

The term atopy comes from Greek and means 'without place'. Because of this meaning, in 1923 Coca and Cooke chose it to describe a condition of altered sensitivity to substances normally present in the environment. Although still a source of debate today, the term atopy is commonly used in medicine to refer to a genetically based tendency to exhibit heightened immune responses to minute amounts of otherwise harmless substances such as pollen, dust mites or food allergens, resulting in the characteristic symptoms of asthma, rhino-conjunctivitis or atopic dermatitis [27].

Epidemiology shows that individuals with a history of atopic skin disease have a tenfold increased risk of developing an occupational skin disease. The fundamental mechanism of this increase is without doubt mainly of an irritative nature [28-29].

For years it was thought that patients had an abnormal adaptive immune response to harmless environmental antigens. Recent studies also highlight the importance of a primary epithelial barrier defect as an initial event with a complex secondary environmental and immunological interaction [30].

In this regard, it has been shown that genetic mutations leading to the formation of filaggrin (FLG), (a protein that guides the proper differentiation of the epidermis, thus ensuring the barrier effect, which plays a key role in preventing dryness and desquamation of the skin, causing excessive trans-epidermal water loss) favour the entry of allergens, antigens, chemical and environmental substances into the body; all of which promote further allergic disorders (food allergy, allergic rhinitis and asthma) playing a role in the so-called atopic march [31].

Skin signs and symptoms	Preventive examination	Periodic visit
Individual hypersusceptibility	<ul style="list-style-type: none"> • Pay attention to activities exposed to irritants or 'wet works'; they do not indicate automatic exclusion from such risk activities; • Adopt the highest degree of environmental and individual protection, schedule close health surveillance. 	<ul style="list-style-type: none"> • Ensure the highest degree of environmental and individual protection, including through the choice of specific PPE; • Implement close periodic health surveillance. • Inform workers adequately of their hypersusceptibility.
Preclinical signs of the disease (sensitisation)	<ul style="list-style-type: none"> • If a sensitisation to a ubiquitous hapten is established, but may lead to other sensitisations, make a proper assessment of the possibility of removing the identified agent; • Intensify environmental and personal prevention, recommending the use of PPE with low sensitising or irritating properties. 	<ul style="list-style-type: none"> • If preclinical signs can be traced back to a hapten present in the work environment, possible substitution of products containing it should be considered and exposure should be limited as much as possible by excluding the worker from activities that expose them most to the identified sensitising agent. • Environmental and personal prevention should be intensified (specific PPE with low sensitising or irritating power), and the frequency of health surveillance visits should be increased.
Specific clinical manifestations	<ul style="list-style-type: none"> • If possible, remove the causative substance or contact with it. 	<ul style="list-style-type: none"> • Remove the substance temporarily until the clinical signs have disappeared completely and reassess in the light of the implementation of environmental and personal prevention (specific PPE); • If signs persist or reappear on resumption of work, assess unfitness for the specific task with reassignment to another activity if possible.

Table 1. Summary of proposed prevention and protection measures according to risk level.

Since atopy, according to the guidelines on occupational contact dermatitis in the general population, has an incidence of more than 20%, it is unrealistic to exclude workers from occupational exposure in the presence of this condition, unless they have obvious symptoms attributable to atopic dermatitis. In the remaining cases, it seems desirable to favour primary and secondary prevention measures [32].

The aim of therapy is to restore the function of the epidermal barrier and reduce the inflammatory state. This can be achieved with hydration, the application of topical anti-inflammatory agents such as corticosteroids and calcineurin inhibitors [33]; it is also functional to use molecules of natural origin to treat the pathology [34].

3.3.2 Extra-occupational skin disorders:

Extra-occupational skin diseases are a wide range of conditions affecting this apparatus, including those caused by bacterial, viral and fungal infections, parasitic infections, allergic reactions and neoplastic conditions [35]. These diseases can act as predisposing conditions or be aggravated by risk factors.

Specifically, they can be classified into:

1. *Predisposing skin conditions:*

- Hand eczema of any kind (DIC, DAC): a predisposing factor for subsequent contact sensitisation and subsequent DAC or contact urticaria (increased skin permeability). A previous DIC that has healed without outcome is not in itself a condition of hypersusceptibility [36].
- Psoriasis: which in the traditional view has a greater capacity for sensitisation, but is not a specific risk factor for ACD.
- Xerosis or follicular keratosis;
- Symptomatic or red dermographism detected;
- Contact urticaria and fibreglass dermatitis;
- Seborrhea, alopecia, seborrheic dermatitis, acne;
- Professional oil for hirsutism and acne.

2. *Pathologies that may be aggravated by exposure to occupational factors:*
 - Seborrheic eczema: from high temperatures and low humidity.
 - Psoriasis: from irritants and even mild traumatism (Koebner's phenomenon is highlighted as a condition in which typical dermatosis lesions appear at the site of the trauma, inflammatory processes).
 - Ichthyosis/hyperkeratosis: from low temperatures and low humidity.
 - Rosacea: from exposure to UV radiation (sunlight or artificial sources).
 - Lichen planus: from dermo-irritants, trauma and repeated microtrauma
 - Urticaria: physical from high or low temperatures, heat, cold, pressure
 - Hyperhidrosis: from prolonged use of gloves (more than 2 hours per day).
3. *Previous skin diseases:* if they have been adequately treated and there have been no recurrences for at least one year without therapy, they are not a factor in hypersusceptibility, except of course for AD and DAC.

3.3.3 Sensitisation from pre-existing contact with haptens and previous exposure and sensitisation to the same risk factor:

Sensitisation is the basic requirement for the clinical expression of allergic contact dermatitis. Allergen molecules entering the body are usually too small to elicit an immune response. However, some ions are chemically reactive (e.g. Ni²⁺) and readily bind proteins, usually negatively charged. The protein-allergen compound, pre-aptene [37], binds the major histocompatibility complex class II (MHC-II), expressed by dendritic and Langerhans cells of the epidermis. (APC).

Some allergens can bind directly to MHC-II without first binding to other proteins or undergoing enzymatic modifications [38].

For activation, maturation and migration of APCs, co-stimulators produced during stress or inflammation must be present, the most important of which are TNF α , IL-1 β and GM-CSF; in their absence the phenomenon of immunological tolerance develops and sensitisation does not occur [39].

Tolerance also tends to develop when the allergen is administered orally, intravenously, or intraperitoneally [40].

Once activated, APCs migrate through afferent lymphatic vessels to the paracortical region of regional lymph nodes. Here they encounter naive T lymphocytes to which they bind via ICAM-1 and LFA-3; the encounter between the two cells is favoured by the structure of the lymph node paracortical region and the dendritic nature of APCs.

Binding results in the secretion of several cytokines, the most important of which are IL-1 from APCs and IL-2 from T lymphocytes. These promote the proliferation of ⁺antigen-specific CD4⁺ and CD8 T lymphocytes, which spill over into the efferent lymphatic vessels and consequently into the blood [41].

The subgroup of CLA⁺ T lymphocytes localises in the skin, especially during inflammation phases, called up by CCL27, a chemokine expressed by basal keratinocytes that binds the CCR10 receptor on lymphocytes.

At this point, cytotoxic T lymphocytes are able to induce cell death in keratinocytes through Fas-ligand or perforins [42].

In the case of strong allergens, a local reaction may occur within 1-4 weeks after contact; this depends on the interaction between the small amount of antigen still present in the skin and the sensitised T lymphocytes, which may persist for months [43]. When a person sensitised to a given allergen comes into contact with it in sufficient concentration, a local reaction develops on average within 24-48 hours, although the interval between exposure and the development of the first lesions may vary from a few hours to four days.

T lymphocytes are also involved in other skin diseases, e.g. T1 lymphocytes are more represented in vitiligo, T17/T22 lymphocytes in psoriasis, regulatory T lymphocytes in melanoma. [44]

For the above, predictive tests can be performed in collaboration with a dermatologist or allergist, the most common of which are skin tests such as the Prick test and Patch test, and the antigen-specific IgE assay [45].

However, these predictive tests should not be carried out on all workers during preventive and periodic medical examinations, as they can in themselves induce sensitisation to the allergens tested and only identify individuals who are already sensitised, but not those who are predisposed to developing skin diseases [46-48].

The performance of such tests is therefore only useful in those in whom there is a well-founded suspicion of an atopic condition, or to ascertain the causes of an inadequately investigated eczematous dermatitis, or to assess those who are to be assigned to an activity with a high risk of exposure [49]

3.3.4 Systemic pathologies

It should be pointed out that various dermatological diseases do not only affect the skin but can also lead to systemic manifestations. It can therefore be said that skin symptoms are the first sign of various systemic diseases such as autoimmune, rheumatological, hepatic or renal diseases.

It is therefore understandable that the diagnostic procedure in dermatoses must include internal knowledge extended to rheumatology, neurology, immunology, etc.

3.4. Objective examination

The history is followed by an objective examination of the entire skin surface, analysing the sites of injury for signs compatible with occupational dermatitis. The most affected areas of the skin are the fingers, hands, arms, neck and face, i.e. the most exposed parts.

3.5. Certificate of fitness for the specific task

The scientific literature does not provide clear and validated guidance on this topic.

A prerequisite for a correct assessment of suitability is defined by a careful analysis and clear aetiological diagnosis of any skin pathology, which must always be made in collaboration with the specialist.

We will then look at the cases where more attention should be paid, in the case of individual hypersusceptibility, to preclinical signs of skin disease or manifest skin manifestations.

- Individual hypersusceptibility: Highlighted during the preventive visit: pay particular attention to activities exposed to irritants or 'wet work' (e.g. hairdressers, cleaners, dishwashers, etc.), adopt the highest degree of environmental and individual protection, schedule close health surveillance. Highlighted during the periodic visit: ensure the highest degree of environmental and individual protection, including through the choice of specific PPE, implement close periodic health surveillance and adequately inform workers of their hypersusceptibility.
- Preclinical signs of the disease (sensitisation): Pre-clinical signs of disease: If sensitisation to a ubiquitous haptene not present in the work environment is established, but may lead to another sensitisation, an appropriate assessment should be made of the possibility of reducing, as far as possible, the subject's exposure to potentially sensitising agents, intensifying environmental and personal prevention and recommending the use of specific PPE.

If preclinical signs can be traced back to a haptene present in the workplace, the possible replacement of products containing it should be considered, and exposure should be limited as much as possible by excluding the worker from activities that most expose him or her to the identified sensitising agent. Finally, environmental and personal prevention should be intensified (specific PPE with low sensitising or irritating power), and the frequency of health surveillance visits should be increased.

- Specific clinical manifestations. Clinical signs of illness with proven sensitisation to haptens in the work environment: if possible, remove the causative substance or contact with it. If this is not possible, temporarily remove the worker until the clinical signs have remitted, in order to carry out a subsequent reassessment in the light of the environmental and personal prevention implemented.

If clinical signs reappear on resumption of work, unfitness for the specific task should be considered with reassignment to another activity where possible.

4. Conclusions

It should be noted that what has been said so far is the result of a summary analysis of possible skin disorders in the occupational setting, highlighting that each case must be assessed individually.

The suitability judgments issued, also with a view to safeguarding the specific professionalism of the employee, should as far as possible resort to measures based on reasoned and feasible 'prescriptions', not limitations equivalent to changes of job and therefore not feasible.

These measures will firstly include assessing the possibility of replacing/removing the aetiological agent, reducing workers' exposure by using appropriate and specific PPE, and carrying out close health surveillance to monitor the effectiveness of any actions taken.

In cases where the chronic clinical picture is particularly serious, the possible transfer of the worker to other activities/occupations should be considered, and if such a conversion is not possible, unfitness for the specific task remains the only admissible instrument.

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